(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 September 2002 (19.09.2002)

PCT

(10) International Publication Number
WO 02/072039 A2

(51) International Patent Classification[7]: A61K 7/00

(21) International Application Number: PCT/EP02/02599

(22) International Filing Date: 8 March 2002 (08.03.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

13/067586	9 March 2001 (09.03.2001)	JP
13/67587	9 March 2001 (09.03.2001)	JP
14/016113	24 January 2002 (24.01.2002)	JP

(71) Applicant *(for all designated States except US)*: **PENTAPHARM LTD** [CH/CH]; Engelgasse 109, CH-4052 Basel (CH).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **YAMAMOTO, Takashi** [JP/JP]; 1-31-12, Yamato-cho, Hachioji-shi, Tokyo (JP). **NAKAYAMA, Hiroki** [JP/JP]; 3-1-4-703, Hyakunin-cho, Shinjuku-ku, Tokyo (JP).

(74) Agent: **BRAUN, André**; Braun & Partner, Reussstrasse 22, CH-4054 Basel (CH).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/072039 A2

Topical dermal and food preparations

(54) Title: TOPICAL DERMAL AND FOOD PREPARATIONS

(57) Abstract: Topical dermal preparation and a food preparation, being suitable for use as a drug, a quasi-drug, a cosmetic, a food or a food additive, said preparation comprizing at least one pyridoxine-α-D-glucoside and optionally α-arbutin and further additives; use of said preparation for preventing or treating rough skin or slowing the ageing of the skin by preventing loss of lustrous complexion from the skin.

Topical dermal and food preparations

The present invention refers to topical dermal preparations and food preparations containing pyridoxine-α-D-glucoside as an active ingredient. These preparations are suitable for use as drugs, quasi-drugs or cosmetics. The topical dermal preparations in particular are useful in preventing or treating rough skin or slowing the ageing of the skin by preventing loss of lustrous complexion from the skin.

Damaged skin is commonly called dry skin or rough skin. Conventionally, dry skin has been treated with topical agents containing moisturizing agents such as hyaluronic acid and various types of ceramide in order to provide water to the corneum, while natural extracts such as aloe, placenta and carrot extracts, allantoin, and fermentation metabolites have been used to deal with rough skin associated with physiological keratinization abnormality.

However, none of these agents is effective enough when topically applied to the skin, and good efficacy cannot be expected. Vitamin B6, or pyridoxine, was discovered as a substance which prevents skin diseases. Its derivatives such as pyridoxine HCl, pyridoxine tripalmitate and pyridoxine dioctanoate have been expected to be effective as topical agents. However, these vitamin B6 derivatives present the problems reported below.

Specifically, pyridoxine HCl is extremely unstable in topical preparations. Pyridoxine tripalmitate and pyridoxine dioctanoate, which are fat-soluble, are not effective enough probably due to their poor solubility in water. Pyridoxine seems to be empirically used in topical

preparations simply because it is believed to be effective in preventing and improving seborrheic dermatitis caused by nutritional deficiency of pyridoxine.

The objective of this invention is to supply topical dermal and food preparations which are pharmaceutically stable and suitable for use as drugs, quasi-drugs or cosmetics which are useful in preventing or treating rough skin or slowing the ageing of the skin by preventing loss of lustrous complexion from the skin.

As a result of studies conducted to achieve the objective mentioned above, the inventors discovered that pyridoxine-α-D-glucoside, a pyridoxine derivative, can be an active ingredient which makes it possible to achieve the objective and have completed this invention.

The present invention is defined in the claims. The present invention particularly refers to a topical dermal preparation and a food preparation, being suitable for use as a drug, a quasi-drug, a cosmetic, a food or a food additive, which are characterized in that said preparations comprize at least one pyridoxine-α-D-glucoside. Said preparations optionally may comprize further additives.

The present invention further refers to the use of said preparation for preventing or treating rough skin or slowing the ageing of the skin by preventing loss of lustrous complexion from the skin.

The present invention further refers to said topical dermal preparations in the form of ointments, creams, poultices, adhesive agents, liquid preparations, aerosols, liniments, and lotions.

The present invention further refers to said food

preparations in the form of a semi-solid, a liquid, or an aerosol, to be used as a food-additive or processed food.

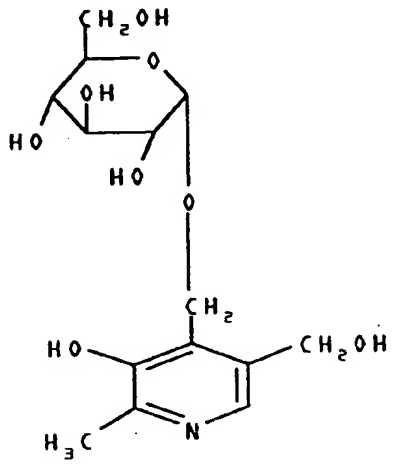
The present preparation may represent a prescribed or a nonprescribed drug, cosmetic or a processed food containing a liquid base.

The present invention further refers to said preparation which further comprizes α-arbutin.

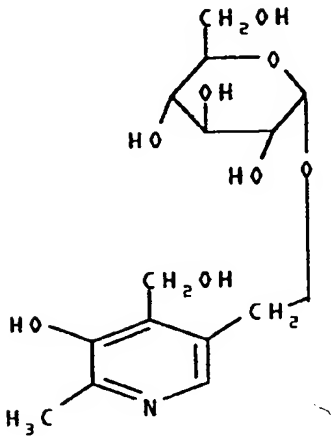
The topical dermal preparations under the present invention preferably contain pyridoxine-α-D-glucoside in an amount of 0.05-20.0% (w/w), and optionally α-arbutin preferably in an amount of 0.05-10.0% (w/w), calculated to the weight of the preparation.

The effect of pyridoxine-α-D-glucoside used in the present invention is different from that expected for pyridoxine conventionally used in topical agents to prevent or improve seborrheic dermatitis caused by nutritional deficiency of pyridoxine; it is used to activate the physiological activity of the skin. Pyridoxine analogues and derivatives used in topical agents described in existing patent gazettes and other documents are pyridoxine HCl, pyridoxine palmitate, pyridoxine dioctanoate, and pyridoxine phosphate as is specifically mentioned in these documents, and not pyridoxine-α-D-glucoside. The topical dermal preparations under the present invention are characterized by the fact that they contain pyridoxine-α-D-glucoside, a pyridoxine derivative different from those described in the existing patent gazettes and other documents.

Pyridoxine-α-D-glucoside has the structural formula shown below.



Pyridoxine-4'-α-D-glucoside



Pyridoxine-5'-α-D-glucoside

As shown above, the present invention uses pyridoxine-4'-α-D-glucoside (PN-4'-G) or pyridoxine-5'-α-D-glucoside (PN-5'-G) alone or as a mixture of any ratio (PN-α-D-G).

Ogata et al and other groups reported methods that use Sarcina or Micrococcus bacteria to produce pyridoxine-α-D-glucoside using sucrose as a sugar donor (K. Ogata et al.: J. Vitaminol., 15, 160-166 (1969); Y. Tani et al.: J. Vitaminol., 15, 167-173 (1969); K. Kawai, et al.: Agric. Biol. Chem., 35 (2), 184-190 (1971), 35 (11), 1660-1661 (1971)), but all these methods were impracticable because of the extremely low yields compared to the large amount of the substrate needed. Subsequently, Suzuki at al (1993) reported a method that produces pyridoxine-α-D-glucoside from Mucor javanicus-derived α-glucosidase using dextrin as a sugar donor with a glucosidization rate of 35% (Y. Suzuki et al.: J. Appl. Glycosci., 43 (3), 369-372 (1996)). This was followed by a report by Suzuki et al. in 1996 that pyridoxine-α-D-glucoside was obtained from

Bacillus macerans or Bacillus stearothermophilus-derived cyclomaltodextringlucanotransferase using dextrin as a sugar donor with a glucosidization rate of 54% or 70% (Y. Suzuki et al.: Noka, 67 (3), 356 (1993); Y. Suzuki, p27-31, proceedings of the 13th Resources Biology Symposium, 1996). However, these methods also do not make it possible to produce practicable amounts of pyridoxine-α-D-glucoside. The authors also failed to suggest its applications.

The inventors have succeeded in establish a commercially useful technology that can be used to produce pyridoxine-α-D-glucoside in an industrial scale (Mem. Grad. School. Sci. & Technol., Kobe Univ., 17-A: 37-45 (1999)). They discovered that the enzymochemical optimal conditions for the production of pyridoxine-α-D-glucoside using the pyridoxine HCl of Bacillus stearothermophilus-derived cyclomaltodextringlucanotransferase (CGTase) as a receptor and maltodextrin as sugar donor is as follows: pH 4.0-8.0, preferably 4.5-5.5 and reaction temperature 30-70°C, preferably 55-65°C. CGTase is also very stable under these conditions. The degree of maltdextrin polymerization should be 4-25, preferably 6-13, and the substrate concentration should be 4-12% for pyridoxine HCl and 0.05-0.10 mol/L for maltdextrin (L, liter; mL, milliliter; μL, micro liter).

The authors produced pyridoxine-α-D-glucoside under these optimal conditions and confirmed that the glucosidization rate of 61%, 67%, and 78% is obtained with the reaction time of 48, 72 and 216 hours.

The reaction fluid also contains pyridoxine-α-maltoglycoside. This is also physicochemically stable and is useful, but the ratio of pyridoxine in the active moiety in its molecule is small. The yield can be increased by converting pyridoxine-α-maltoglycoside contained in the reaction fluid to pyridoxine-α-D-glucoside using glucoamylase

derived from Rhizopus sp. such as Rhizopus niveus, Saccharomycopsis fibuligera, and Candida tsukubaensis.

In order to economically manufacture pyridoxine-α-D-glucoside, it is possible to use immobilization technology to recover CGTase from the reaction fluid or to conduct continuous production using an immobilized CGTase column reactor to increase the production efficiency. Pyridoxine-α-D-glucoside obtained by the above-mentioned enzymatic methods can be purified as shown below.

The reaction fluid obtained in the production of pyridoxine-α-D-glucoside from Bacillus stearothermophilus-derived CGTase under the optimal conditions shown above using commercial pyridoxine HCl as a receptor and commercial maltdextrin as a sugar donor contains pyridoxine which has not yet reacted. This reaction fluid can be completely separated into pyridoxine and pyridoxine-α-D-glucoside (PN-α-D-G) by treating it by gel filtration column chromatography (using fillers such as Sephadex LH-20 (Pharmacia Biotech)) using an appropriate solvent (such as 20% methanol). This separation procedure may be repeated to increase the purity although one cycle is sufficient.

The separated product is a 2:1 mixture of PN-4'-G and PN-5'-G on a molar basis. These two ingredients can be separated, if necessary, by treating the mixture by column chromatography using an appropriate solvent. Usable methods include Cosumosil 75C18-OPN (Nacalai Tesque) column chromatography using 10% ethanol and Dowex 50Wx8 (Dow Chemical) column chromatography using formic acid-ammonium formate buffer solution containing 40% ethanol. Operations should be repeated to increase purity.

Basically, the separation and purification methods described above can be applied to pyridoxine-α-D-glucoside

produced by Bacillus stearothermophilus-derived CGTase and Bacillus macerans-derived α-glucosidase.

Results of FABMAS (JEOL Ltd., JMX-AX505W) analysis suggest that the molecular weight of both ingredients is 331, and this is equivalent to the theoretical value, but the identification of PN-4'-G and PN-5'-G can be easily done based on the assignment of each signal on the ^{1}H-NMR spectrum. The ^{1}H-NMR spectrum of PN-4'-G and PN-5'-G determined at 25°C and 400 MHz (JEOL Ltd., JNX-EX400W) is as reported below.

In the chemical shift of PN-4'-G, the singlet signal at 7.87 ppm is assigned to the proton directly bound to position 6 of pyridoxine; the doublet signal at 4.87 ppm to one of the two protons at position 4' of pyridoxine; the doublet signal at 4.74 ppm to the proton at position 1' of glucose; the double signal at 4.53 ppm to another proton at position 4' of pyridoxine; the singlet signal at 4.46 ppm to 2 protons at position 5' of pyridoxine; the multiplet signal at 3.59-3.06 ppm to 6 protons at positions 2', 3', 4', 5' and 6'; and the singlet signal at 2.30 ppm to 3 protons at position 2' of pyridoxine.

The fact that protons of the hydroxymethyl group at position 4 of pyridoxine are not equivalent and are found separated into 2 signals indicates that the glucose is bound at position 4' and that PN-4'-G is α-bound with the anomeric proton of glucoside showing a small coupling constant (J: 3.4Hz). Likewise, the assignment of major signals on the ^{1}H-NMR spectrum of the other ingredient is as follows: the singlet at 4.76 ppm is assigned to 2 protons at position 4' of pyridoxine; the doublet at 4.69 ppm to one of the 2 protons at position 5' of pyridoxine; and the doublet at 4.48 ppm to the other proton at position 5' of pyridoxine. The fact that protons of the hydroxymethyl group at position 5 of pyridoxine are not

equivalent and are found separated into 2 signals indicates that the glucose is bound at position 5' and that PN-5'-G is α-bound with the anomeric proton of glucoside showing a small coupling constant (J: 3.4Hz).

The content of pyridoxine-α-D-glucoside in topical dermal preparations under the present invention is not specified and can be set at any level depending on their intended applications. In general, however, it is desirable to be 0.05-20.0% (w/w).

In addition to pyridoxine-α-D-glucoside, additives commonly used in the production of drugs, quasi-drugs and cosmetics for topical application can be added to the topical dermal preparations under the present invention, such as moisturizing agents, UV protecting agents, whitening agents, antioxidants, viscosity donors, surface active agents, alcohol, aqueous ingredients, pigments, sequestrants, and skin nutrients.

It is also possible to add, with or without these additives, whitening agents such as arbutin, α-arbutin (hydroquinone-α-D-glucoside), 4-n-butylresorcinol, ascorbic acid, magnesium phosphate ascorbate, glucoside ascorbate, kojic acid, glucoside kojiate, and placenta extract, various crude drugs, ceramide, substances with ceramide-like structures, pantlacton, pantethine, pantethine-S- sulfonate and its salts, GABGA, epsilon-aminocaproic acid, tranexamic acid, vitamin E and its esters or derivatives, glycyrrhetic acid and its derivatives or salts, and saccharide such as trehalose.

Topical dermal preparations, therefore, may contain pyridoxine-α-D-glucose and at least one compound selected from ascorbic acid and its derivatives, galenicals and their extracts, hydroxycarboxylic acid and its salts, oil-soluble *Glycyrrhiza* extracts, gentian extracts, phenol

derivatives and their salts, placenta extracts, kojic acid and its derivatives, glucosamine and its derivatives, azelaic acid and its derivatives, retinol and its derivatives, hydroquinone glycoside, tocopherol and its derivatives, vitamin E-nicotinate, diisopropylamine dichloroacetate, chitosan and its degradation products, caffeic acid derivatives, hydroxycinnamic acid and its derivatives, *Umbelliferae* extracts, mycelial culture and its extracts, plant leaves and their extracts, plant stem bark and its extracts, hinokitiol, ginseng extracts, sulfur, crude sugar extracts, molasses extracts, mucopolysaccharides, teprenone, nordihydroguaiaretic acid, UV-absorbers, γ-pyrone glycoside, hydroxy-salicylic acid glycoside, hydroxysalicylic acid aliphatic ester glycoside, biphenyl compounds, ceramides, ceramide analogues, ether compounds described in a general formula of R_1-O-(X-O)n-R_2 (wherein R_1 and R_2 are identical or different and represent a C_{1-12} straight chained, branched or cyclic alkyl group, X being C_{1-12} alkylene group, n being 0 or 1, and the total C-number of R_1, R_2 and X being 10-32), pantothenic acid and its derivatives, sodium hydrogen sulfite, antiphlogistics, allantoin and its derivatives, amino acids and their derivatives, aminoethyl compounds, alkylenediaminecarboxylic acid derivatives, betaine derivatives, acylmethyltaurine, fibronectine, anti-tyrosinase activators, hederacocide and its salts, gymnema saponin and its salts, beet saponin and its salts, ellagic acid-type compounds and their alkali metal salts, resorcinol derivatives, dihydroxyacetone and its derivatives, and S-1,2,3,4-trihydroxy-2-butane and its derivatives.

The pyridoxine-α-D-glucoside may be, as described above, pyridoxine-4-α-D-glucoside or pyridoxine-5'-α-D-glucoside alone or a mixture thereof at any mixing ratio.

Preparations or foods that contain pyridoxine glycoside, as mentioned above, contain pyridoxine-α-D-glucoside, and may be semi-solid, liquid or aerosol-type prescribed or non-prescribed drugs, cosmetics or processed foods. These preparations or foods may represent prescribed or non-prescribed drugs, cosmetics or processed foods which contain a liquid base.

When using α-arbutin, it is recommended that pyridoxine-α-D-glucoside be added at 0.05-20.0% (w/w) and α-arbutin at 0.05-10.0% (w/w). At these concentrations, the desirable effects of pyridoxine-α-D-glucoside and α-arbutin on the skin are not affects. On the contrary, their effects are enhanced and their ability to prevent or improve rough skin and slow down the skin ageing process by preventing the loss of lustrous complexion of the skin is increased.

The topical dermal preparations under the present invention that contain the above-mentioned ingredients can be manufactured in known manner and with known methods in various dosage forms such as ointment, cream, poultices, adhesive agents, liquid preparations, aerosol, liniments, and lotion. The following Examples illustrate the present invention.

Example 1

A mixture of purified water and propylene glycol was prepared at the ratio shown in Table 1, and PN-α-D-G, methyl parahydroxybenzoate and butyl parahydroxybenzoate were added at the ratio shown in Table 1. The mixture was then dissolved by heating at 80°C.

To the solution obtained, a mixture of all other ingredients prepared at the ratio shown in Table 1 and dissolved by heating at 80°C was added little by little, and the mixture was rapidly emulsified using a homo-mixer. The emulsion was gradually cooled to prepare ointment.

Table 1 (wt%)

PN-α-D-G*	:	10.0
Petrolatum	:	4.0
Stearyl alcohol	:	5.0
Liquid paraffin	:	17.0
POE (20) cetyl ether	:	4.0
Glycerin monostearate	:	2.0
Methyl parahydroxybenzoate	:	0.1
Butyl parahydroxybenzoate	:	0.1
Propylene glycol	:	5.0
Purified water	:	q.s.

* 2:1 mixture of PN-4'-G and PN-5'-G on a molar basis

Example 2

PN-α-G was dissolved in purified water at the ratio shown in Table 2, and the solution obtained was heated to and maintained at 70°C. The solution obtained was added to a mixture of all other ingredients prepared at the ratio shown in Table 2 and dissolved by heating at 70°C and maintained at this temperature. The mixture obtained was thoroughly stirred and cooled to prepare a cream.

Table 2 (wt%)

PN-α-D-G*	:	5.0
Polyethylene glycol isostearate	:	4.0
Cetanol	:	1.0
Liquid paraffin	:	7.5
Isopropyl myristate	:	7.5
Diethylene glycol monomethyl ether	:	10.5
Ester parahydroxybenzoate	:	0.5
Propylene glycol	:	5.0
Purified water	:	q.s.

* Same as that used in Example 1

Example 3

PN-α-G was dissolved in purified water at the ratio shown in Table 3, and the solution obtained was heated to and maintained at 70°C. The solution obtained was added to a mixture of all other ingredients prepared at the ratio shown in Table 3 and dissolved by heating at 70°C and maintained at this temperature. The mixture obtained was thoroughly stirred, cooled to 50°C, homogenized, and then cooled to 30°C. Locust bean gum was added to the homogenate at the ratio shown in Table 3, stirred, and cooled to prepare a cream.

Table 3 (wt%)

PN-α-D-G*	:	5.0
Polyoxyethylene sorbitan monostearate	:	4.0
Sorbitan monostearate	:	3.0
Glycerin monostearate	:	2.0
Cetanol	:	2.5
Isopropyl myristate	:	8.0
Ester parahydroxybenzoate	:	0.5
Propylene glycol	:	2.0
Locust bean gum	:	2.0
Purified water	:	q.s.

* Same as that used in Example 1

Test 1

Sample A containing 5.0% (w/w) PN-α-D-G (same as used in Working Example 1), Sample B containing 5.0% (w/w) placenta extract (manufactured by Pentapharm Corporation), and Sample C not containing either PN-α-D-G or placenta extract were prepared in accordance with the formula of the cream prepared in Working Example 2. The ability of these preparations to improve rough skin and rash caused by shaving was evaluated as mentioned below.

Improvement of rough skin

The test was conducted in 50 female volunteers with rough skin. Sample A or B was applied to the cheek on one side and Sample C containing no active ingredient was applied to the cheek on the other side. About 0.3 g was applied twice a day for 3 weeks. The skin condition was examined and evaluated after completion of the treatment. Findings obtained are reported in Table 4. The efficacy was classified into one of the following 4 categories:

Markedly effective: symptoms disappeared and the skin recovered lustrous complexion.

Effective: symptoms were relieved and the skin recovered lustrous complexion.

Slightly effective: symptoms were slightly relieved and skin recovered lustrous complexion.

Ineffective: symptoms were not relieved.

Table 4

	Sample A	Sample B	Sample C
Markedly effective	8	4	0
Effective	10	4	4
Slightly effective	3	10	20
Ineffective	4	7	26

As shown in Table 4, the cream containing pyridoxine-α-D-glucoside showed marked efficacy for rough skin.

Test 2

The test was conducted in 45 male volunteers with rash due to shaving divided into 3 groups of 15 volunteers. Volunteers were asked to shave once a day and apply Sample A, B or C immediately after shaving. The test was conducted for 1 week and the effect of the samples on rash due to shaving was examined. Findings obtained are reported in Table 5. The efficacy was classified into one of the following 4 categories:

Markedly effective: no rash occurred due to shaving.

Effective: rash due to shaving was relieved.

Slightly effective: rash due to shaving was relieved to some extent.
Ineffective: rash due to shaving was not relieved.

Table 5

	Sample A	Sample B	Sample C
Markedly effective	4	2	0
Effective	5	4	1
Slightly effective	4	6	5
Ineffective	2	3	9

As shown in Table 5, the cream containing pyridoxine-α-D-glucoside was effective for rash due to shaving.

Test 3

The stability of the cream prepared as shown in Working Example 2 was determined using the volumes shown below in order to evaluate the stability of topical dermal preparations under the present invention.

A topical dermal preparation containing 0.5% (w/w) PN-α-D-G was prepared using the formula shown in Working Example 2. The cream obtained was transferred into plastic containers, 10g per container, packed in aluminum foil, and kept at constant temperature of 50°C for 0, 30 and 90 days (accelerated stability study), and the stability was evaluated. A cream containing pyridoxine HCl at 0.5% (w/w; final concentration) as pyridoxine, in place of PN-α-D-G, was used as control.

The pH value of both test cream and control cream was adjusted to 6.0 by dropping 0.1N NaOH at the final stage of preparation. Stability was evaluated based on quantitative analysis of pyridoxine HCl, PN-4'-G and PN-5'-G.

For quantitative analysis, 1 g was taken from the sample containers 0, 30 and 90 days after starting the test, thoroughly suspended in 10 volumes of purified water, allowed to stand 4 hours at a cool place (4°C), and filtered. Two μL each of the filtrate was sampled and subjected to HPLC. HPLC was conducted using a Hitachi L-6200 pump system, a Hitachi 655A-52 column oven, a Hitachi F-2250 fluorescence detector, and a Hitachi D-2500 data processor. A 0.5:99.5 (v/v) mixture of methanol in water was used as mobile phase. The flow rate was 1.0 mL/min and the column temperature was 30°C. The peak area comparison method was used for assay.

The retention time for pyridoxine HCl (as pyridoxine), PN-4'-G, and PN-5'-G was 14, 18 and 31 min, respectively. The residual amount was determined from the previously drawn standard curve. Findings obtained are shown in Table 6.

Data presented in Table 6 are means of values determined in triplicate and show residual percentages for PN-α-D-G (sum or PN-4'-G and PN-5'-G) and pyridoxine.

Table 6

	Day 0	Day 30	Day 90
A) Invention	100.0	100.1	98.9
B) Control	100.0	89.8	67.1

Effects of the invention

The following effects can be obtained with topical dermal preparations under the present invention:

1) Because pyridoxine-α-D-glucoside under the present invention is compatible with many ingredients, it can be easily formulated into topical dermal preparations for use as drugs, quasi-drugs and cosmetics.
2) In a clinical trial in volunteers, pyridoxine-α-D-glucoside was confirmed to be effective in preventing

and improving rough skin and slowing down the ageing of the skin by preventing loss of lustrous complexion.

3) In a clinical trial in volunteers liable to rash due to shaving, pyridoxine-α-D-glucoside was confirmed to effectively prevent rash due to shaving.

Claims

1. Topical dermal preparation and a food preparation, being suitable for use as a drug, a quasi-drug, a cosmetic, a food or a food additive, characterized in that said preparation comprizes at least one pyridoxine-α-D-glucoside.

2. Preparation according to claim 1, characterized in that said preparation further comprizes α-arbutin.

3. Preparation according to claim 1, characterized in that said preparation comrpizes pyridoxine-α-D-glucoside in an amount of 0.05-20.0% (w/w), calculated to the weight of the preparation.

4. Preparation according to claim 3, characterized in that said preparation further comprizes α-arbutin in an amount of 0.05-10.0% (w/w), calculated to the weight of the preparation.

5. Preparation according to any of the claims 1-3, characterized in that said preparation comprizes pyridoxine-4'-α-D-glucoside or pyridoxine-5'-α-D-glucoside or as a mixture thereof in any ratio.

6. Preparation according to any of the claims 1-5 in the form of a drug, a quasi-drug or a cosmetic for topical application, further comprizing at least one additive selected from the following additives: moisturizing agents, UV protecting agents, whitening agents, antioxidants, viscosity donors, surface active agents, alcohols, aqueous ingredients, pigments, sequestrants, and skin nutrients.

7. Preparation according to any of the claims 1-5 in the form of a drug, a quasi-drug or a cosmetic for topical

application, further comprizing at least one additive selected from the following additives: whitening agents, preferably arbutin, α-arbutin, 4-n-butylresorcinol, ascorbic acid, magnesium phosphate ascorbate, glucoside ascorbate, kojic acid, glucoside kojiate, placenta extract, various crude drugs, ceramide, substances with ceramide-like structures, pantlacton, pantethine, pantethine-S- sulfonate and its salts, GABGA, epsilon-aminocaproic acid, tranexamic acid, vitamin E and its esters or derivatives, glycyrrhetic acid and its derivatives or salts, and saccharide preferably trehalose.

8. Topical dermal preparation according to any of the calims 1-7, characterized in that said preparation further comprizes at least one compound selected from ascorbic acid and its derivatives, galenicals and their extracts, hydroxycarboxylic acid and its salts, oil-soluble *Glycyrrhiza* extracts, gentian extracts, phenol derivatives and their salts, placenta extracts, kojic acid and its derivatives, glucosamine and its derivatives, azelaic acid and its derivatives, retinol and its derivatives, hydroquinone glycoside, tocopherol and its derivatives, vitamin E-nicotinate, diisopropylamine dichloroacetate, chitosan and its degradation products, caffeic acid derivatives, hydroxycinnamic acid and its derivatives, *Umbelliferae* extracts, mycelial culture and its extracts, plant leaves and their extracts, plant stem bark and its extracts, hinokitiol, ginseng extracts, sulfur, crude sugar extracts, molasses extracts, mucopolysaccharides, teprenone, nordihydroguaiaretic acid, UV-absorbers, γ-pyrone glycoside, hydroxy-salicylic acid glycoside, hydroxysalicylic acid aliphatic ester glycoside, biphenyl compounds, ceramides, ceramide analogues, ether compounds described in a general formula of R_1-O-(X-O)n-R_2 (wherein R_1 and R_2 are identical or different and represent a C_{1-12} straight chained, branched or cyclic alkyl group, X being C_{1-12} alkylene group, n being 0 or 1, and the total

C-number of R_1, R_2 and X being 10-32), pantothenic acid and its derivatives, sodium hydrogen sulfite, antiphlogistics, allantoin and its derivatives, amino acids and their derivatives, aminoethyl compounds, alkylenediaminecarboxylic acid derivatives, betaine derivatives, acylmethyltaurine, fibronectine, anti-tyrosinase activators, hederacocide and its salts, gymnema saponin and its salts, beet saponin and its salts, ellagic acid-type compounds and their alkali metal salts, resorcinol derivatives, dihydroxyacetone and its derivatives, and S-1,2,3,4-trihydroxy-2-butane and its derivatives.

9. Preparation according to any one of the claims 1-8 in the form of a semi-solid, a liquid or an aerosol-type, prescribed or non-prescribed drug, a cosmetic or a processed food optionally containing a liquid base.

10. Preparation according to any one of the claims 1-9 in the form of an ointment, a cream, a poultices, an adhesive agent, a liquid preparation, an aerosol, a liniment, or a lotion.

11. The use of a preparation according to any one of the claims 1-10, for preventing or treating rough skin or slowing the ageing of the skin by preventing loss of lustrous complexion from the skin.

12. Preparation in the form of a food, a food-additive or a processed food, according to any one of the claims 1-8 in the form of a semi-solid, a liquid, or an aerosol.